

## Patent claims

1. Use of affinity-purified polyclonal human autoantibodies against the TSH receptor (TSHR-Auto-Ab) from sera of Graves' disease patients, and/or of animal antibodies which compete with these for binding sites of a functional human TSH receptor, as a specific binding reagent in an immunological assay method for clinical identification of autoantibodies against the TSH receptor (TSHR-Auto-Ab) in a sample of a biological fluid of a patient to be investigated for Graves' disease.
- 15 2. Use according claim 1, wherein the affinity-purified polyclonal human autoantibodies against the TSH receptor (TSHR-Auto-Ab) are purified to biochemical homogeneity and have a specific activity of at least 1 IU/mg of protein (human immunoglobulin).
- 20 3. Use according to claim 1 or 2, wherein the affinity-purified polyclonal human autoantibodies against the TSH receptor (TSHR-Auto-Ab) were obtained by purification by affinity chromatography, in which the autoantibodies from a pool of sera of Graves' disease patients were bound to an affinity material having a functional human recombinant TSH receptor bound thereto, washed protein-free and then eluted from the affinity material.
- 25 30 4. Use according to claim 1, wherein the animal

antibodies which compete with the affinity-purified polyclonal human autoantibodies against the TSH receptor (TSHR-Auto-Ab) from sera of Graves' disease patients were selected by allowing animal monoclonal antibodies against a human or animal TSH receptor, or against individual segments of such a receptor, to compete with labelled affinity-purified polyclonal human autoantibodies against the TSH receptor (TSHR-Auto-Ab) from sera of Graves' disease patients for binding sites of a human TSH receptor, and using those monoclonal antibodies which show such competition, alone or in a mixture with other competing antibodies, as a specific binding reagent in an immunological assay method for the clinical identification of autoantibodies against the TSH receptor (TSHR-Auto-Ab) in a sample of biological fluid.

5. Use according to any of claims 1 to 4, wherein the affinity-purified polyclonal human autoantibodies against the TSH receptor (TSHR-Auto-Ab) from sera of Graves' disease patients, and/or the animal antibodies which compete with the former, are used in directly or indirectly labelled form in a competitive immunological assay method as competitors for the autoantibodies against the human TSH receptor which are to be determined in a sample of a patient.

30 6. Use according to any of claims 1 to 5, wherein the immunological assay method is a competitive method in which a preparation of a functional recombinant

human TSH receptor in a form bound to a solid phase or in solubilized form is used as a specific binding partner for the autoantibodies to be determined and the affinity-purified polyclonal human autoantibodies against the TSH receptor (TSHR-Auto-Ab) used as competitors and obtained from sera of Graves' disease patients, and/or animal antibodies which compete with these.

- 10 7. Use according to any of claims 1 to 4, wherein the affinity-purified polyclonal human autoantibodies against the TSH receptor (TSHR-Auto-Ab) from sera of Graves' disease patients, and/or the animal antibodies which compete with these for binding sites of a functional human TSH receptor, are used in a form bound to the solid phase, and a solubilized functional human recombinant TSH receptor in directly or indirectly labelled form is used as a specific binding partner.
- 20 8. Use according to claim 5, characterized in that the affinity-purified polyclonal human autoantibodies against the TSH receptor (TSHR-Auto-Ab) from sera of Graves' disease patients, and/or the animal antibodies which compete with these for binding sites of a functional human TSH receptor, are used in a form labelled with a radio isotope, a chemiluminescent label or a fluorescent label or with the aid of a correspondingly labelled animal anti-human IgG.
- 25 30 9. Reagent kit for clinical diagnosis for the immunological determination of autoantibodies

against the TSH receptor in patient sera, which, in addition to the customary components, such as, in particular, dilution and/or buffer solutions, standards and zero standard and optionally control sera, contains, as two further components, a human TSH receptor which is solubilized or bound to a solid phase and a labelled preparation of affinity-purified polyclonal human autoantibodies against the TSH receptor (TSHR-Auto-Ab) from sera of Graves' disease patients, and/or of animal antibodies which compete with these for binding sites of a functional human TSH receptor.

10. Method for the selection of monoclonal animal antibodies which compete with autoantibodies from the sera of Graves' disease patients for binding sites of the functional human TSH receptor, in which the culture supernatants of hybridomas which express antibodies against the TSH receptor are allowed to compete with labelled affinity-purified polyclonal human autoantibodies against the TSH receptor (TSHR-Auto-Ab) from sera of Graves' disease patients for the binding sites of a functional human TSH receptor, and monoclonal antibodies having the desired competition properties are recognized and selected on the basis of the weakening of the binding of the labelled autoantibodies.
15. Affinity-purified polyclonal human autoantibodies against the TSH receptor (TSHR-Auto-Ab) from sera of Graves' disease patients which are purified to biochemical homogeneity and have a specific

activity of at least 1 IU/mg of protein (human immunoglobulin), in labelled form.

- 5       12. Selected animal antibodies which compete with affinity-purified polyclonal human autoantibodies against the TSH receptor (THSR-Auto-Ab) from sera of Graves' disease patients for binding sites of a functional human TSH receptor, in labelled form.